

AMENDMENT AND RESPONSE

Serial Number: 09/096,749

Filing Date: June 12, 1998

Title: ARTIFICIAL ANTIBODY POLYPEPTIDES

Page 2

Dkt: 109.034US1

On page 47, line 15, please replace "Felix" with -- FELIX--, and "nmrPipe" with -- NMRPIPE--.

On page 49, line 21, please replace "Quanta" with -- QUANTA--.

On page 53, line 29, please replace "Hi-Trap" with --HI-TRAP--.

On page 54, line 3, please replace "ResourceS" with --RESOURCES®--.

On page 57, line 24, please replace "NMRPipe" with --NMRPIPE--, and at line 25 please replace "NMRView" with --NMRVIEW--.

On page 12, please replace lines 7-12 with the following text:

--**Figure 1A.**  $\beta$ -Strand and loop topology of anti-lysozyme immunoglobulin D1.3. (Bhat et al., 1994) The locations of complementarity determining regions (CDRs, hypervariable regions) are indicated.

**Figure 1B.**  $\beta$ -Strand and loop topology of the 10th type III domain of human fibronectin. (Main et al., 1992) The locations of the integrin-binding Arg-Gly-Asp (RGD) sequence is indicated.

**Figure 1C.** MOLSCRIPT representation of anti-lysozyme immunoglobulin D1.3. (Kraulis, 1991; Bhat et al., 1994) The locations of complementarity determining regions (CDRs, hypervariable regions) are indicated.

**Figure 1D.** MOLSCRIPT representation of the 10th type III domain of human fibronectin. (Kraulis, 1991; Main et al., 1992) The locations of the integrin-binding Arg-Gly-Asp (RGD) sequence is indicated.--

On page 12, please replace lines 20-22 with the following text:

--**Figure 3A.** Far UV CD spectra of wild-type Fn3 at 25°C and 90°C. Fn3 (50  $\mu$ M) was dissolved in sodium acetate (50 mM, pH 4.6).

**Figure 3B.** Thermal denaturation of Fn3 monitored at 215 nm. Temperature was increased at a rate of 1°C/min.--

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Please replace the text on page 12, line 23 to page 13, line 4 with the following text:

--**Figure 4A.** C $\alpha$  trace of the crystal structure of the complex of lysozyme (HEL) and the Fv fragment of the anti-hen egg-white lysozyme (anti-HEL) antibody D1.3 (Bhat et al., 1994). Side chains of the residues 99-102 of VH CDR3, which make contact with HEL, are also shown.

**Figure 4B.** Contact surface area for each residue of the D1.3 VH-HEL and VH-VL interactions plotted vs. residue number of D1.3 VH. Surface area and secondary structure were determined using the program DSSP (Kabsh and Sander, 1983).

**Figure 4C.** Schematic drawings of the  $\beta$ -sheet structure of the F strand-loop-G strand moieties of D1.3 VH. The boxes denote residues in  $\beta$ -strands and ovals those not in strands. The shaded boxes indicate residues of which side chains are significantly buried. The broken lines indicate hydrogen bonds.

**Figure 4D.** Schematic drawings of the  $\beta$ -sheet structure of the F strand-loop-G strand moieties of Fn3. The boxes denote residues in  $\beta$ -strands and ovals those not in strands. The shaded boxes indicate residues of which side chains are significantly buried. The broken lines indicate hydrogen bonds.--

Please replace the text on page 14, lines 13-23 with the following text:

**Figure 15A.** Characterization of the binding reaction of Ubi4-Fn3 to the target, ubiquitin. Phage ELISA analysis of binding of Ubi4-Fn3 to ubiquitin. The binding of Ubi4-phages to ubiquitin-coated wells was measured. The control experiment was performed with wells containing no ubiquitin.

**Figure 15B.** Competition phage ELISA of Ubi4-Fn3. Ubi4-Fn3-phages were preincubated with soluble ubiquitin at an indicated concentration, followed by the phage ELISA detection in ubiquitin-coated wells.

**Figure 15C.** Competition phage ELISA testing the specificity of the Ubi4 clone. The Ubi4 phages were preincubated with 250  $\mu$ g/ml of soluble proteins, followed by phage ELISA as in (b).

**Figure 15D.** ELISA using free proteins.--